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PHYSICOCHEMICAL CHARACTERIZATION OF RIBAVIRIN WITH SPECTROSCOPY AND MOLECULAR MODELING

K. I. Kienskaya, M. F. Bobrov, A. M. Kusmaev, A. V. Krivitskaya, T. U. Koldaeva, M. V. Sardushkin, R. R.Ibragimova, I. A. Belova, A. V. Kukharenko, G. T. Mazitova, Y. V. Ermolenko and O. V. Zavyalova*

Technology of Chemical and Pharmaceutical and Cosmetic Products Division; D.I. Mendeleev University of Chemical Technology of Russia; 125047, Moscow, Miusskaya Sq. 9, Russia
**Collegium Medicum im. Ludwika Rydygiera w Bydgoszczy, ul. Jagiellońska 13-15, Bydgoszcz, 85-067 Poland.* Tel.: 8 903 1166017. E-mail: kienskaya@muctr.ru

Abstract. Ribavirin - (1-beta-D-ribofuranosyl-1H-1,2,4 triazole-3-carboxamine) inhibits the replication of RNA and DNA viruses. In combination with interferon-α used to treat hepatitis C virus, however the mechanism of their synergetic effect is not established [1].

The aim of the present work was to study the interaction with ribavirin and interferon in aqua phase. Ribavirin (99,8%) was obtained from Fluka (USA); interferon-alpha-2b was kindly obtained from Biocad Company (Russia, S-Petersburg).

Interferon-ribavirin interactions were studied using affinity capillary electrophoresis (ACE); CD - measurements were recorded on Chirascan–Plus spectrometer.

CD spectroscopic technique is useful in monitoring the conformational variations of Interferon in solutions. Our investigations showed that in the presence of ribavirin from 0,14 mMol to 2.98 mMol in mixture solution the quantity of Helix 1 decreased (from 0,38 to 0,27), but quantity of Helix 2 remained constant – about 0,20 (Fig 1).

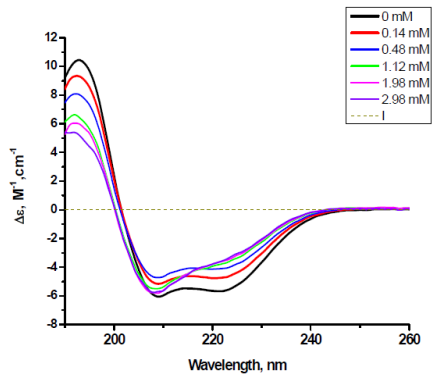

Fig.1. CD-spectra of mixed solutions Ribavirin-Interferon

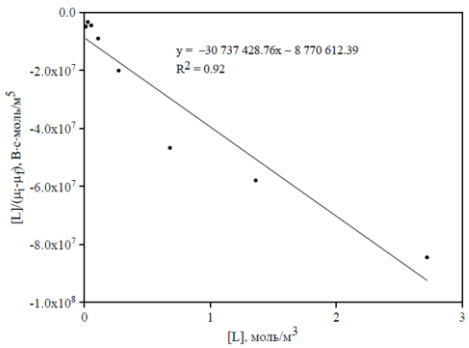

Fig.2. Scatchard plot of Ribavirin-Interferon interaction from binding profile data using ACE.

The experimental data were approximated by the Hill-model: Complex portion = $x^n/(x^n + K_d)$, где $K_d = k_{assoc}./k_{dissoc}. = (K_D)^n$. The caclculated constant by the CD-methos was $K_D = 0.16\pm0.01$ mM; n = 1.3±0.1

Graphical analysis of the profile (ACE-measurements) is show in Fig.2, resulting in one distinct linear plot. The binding constant was calculated by ACE-method with correlation coefficient 0,92. K_D = 0.285 mM.

These studies may provide a rapid approach for the determination of binding constant RibavirinInterferon and provide some analytical insight into synergetic effect of Ribavirin-Interferon mixture in drug compositions.

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References

[1] Ghany M. G., Nelson D. R., Strader D. B., et al. (2011). *Hepatology*. Vol. 54, № 4. – pp. 1433–1444.